[Federal Register: May 17, 1994]

Part V

Department of Health and Human Services

Centers for Disease Control and Prevention

Preventing the Spread of **Vancomycin** Resistance--Report From the Hospital Infection Control Practices Advisory Committee; Comment Period and Public Meeting; Notice
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

Preventing the Spread of **Vancomycin** Resistance--A Report From the Hospital Infection Control Practices Advisory Committee Prepared by the Subcommittee on Prevention and Control of Antimicrobial-Resistant Microorganisms in Hospitals; Comment Period and Public Meeting

AGENCY: Centers for Disease Control and Prevention (CDC), Public Health Service (PHS), Department of Health and Human Services (DHHS).

ACTION: Notice.

SUMMARY: This notice is a request for review and comment of the draft document, Preventing the Spread of **Vancomycin** Resistance--A Report From the Hospital Infection Control Practices Advisory Committee (HICPAC) Prepared by the Subcommittee on Prevention and Control of Antimicrobial-Resistant Microorganisms in Hospitals. The draft document was prepared in collaboration with the National Center for Infectious Diseases (NCID), CDC, and representatives of the American Hospital Association, American Society for Microbiology, Association for Professionals in Infection Control and Epidemiology, Infectious Diseases Society of America, Society for Healthcare Epidemiology of America, and Surgical Infection Society.

DATES: Written comments on the draft document must be received on or before July 18, 1994.

ADDRESSES: Comments on this document should be submitted in writing to the Centers for Disease Control and Prevention (CDC), Attention: VRE Report Center, Mailstop A-07, 1600 Clifton Road, NE., Atlanta, Georgia 30333. The Federal Register containing this draft document may be viewed and photocopied at most libraries designated as U.S. Government Depository Libraries and at many other public and academic libraries that receive the Federal Register throughout the country. In addition, copies of this Federal Register notice document can be obtained by calling (404) 332-2569.

FOR FURTHER INFORMATION CONTACT: The VRE Report Center, telephone (404) 332-2569.

SUPPLEMENTARY INFORMATION: A public meeting for an open discussion of the draft document will be held at the CDC, Atlanta, Georgia, on June 15, 1994. Details about the meeting will be announced in a forthcoming issue of the Federal Register.

Dated: May 11, 1994.
Claire V. Broome,
Acting Deputy Director, Centers for Disease Control and Prevention (CDC).

Appendix--Preventing the Spread of **Vancomycin** Resistance-- A Report from the Hospital Infection Control Practices Advisory Committee Prepared by the Subcommittee on Prevention and Control of Antimicrobial-Resistant Microorganisms in Hospitals

Executive Summary

This document contains recommendations for the prevention and control of the spread of **vancomycin** resistance, with special focus on **vancomycin**-resistant enterococci (VRE).

A rapid increase in the incidence of infection and colonization with VRE has been reported from U.S. hospitals in the last 5 years. This increase poses several problems, including (a) the lack of available antimicrobial(s) for therapy of infections due to VRE, since most VRE are also resistant to multiple other drugs, e.g., aminoglycoside and ampicillin, previously used for treatment of infections due to these organisms; and (b) the possibility that the **vancomycin**-resistance genes present in VRE may be transferred to other gram-positive microorganisms such as Staphylococcus aureus.

An increased risk of VRE infection and colonization has been associated with previous **vancomycin** and/or multi-antimicrobial therapy, severe underlying diseases or immunosuppression, and cardio-thoracic or intraabdominal surgery. Because enterococci can be found in the normal gastrointestinal or female genital tracts, most enterococcal infections have been attributed to endogenous sources within the individual patient. However, recent reports of outbreaks and endemic infections due to enterococci, including VRE, have shown that patient-to-patient transmission of the microorganisms can occur either via direct contact or indirectly via hands of personnel or contaminated patient-care equipment or environmental surfaces.

Prevention and control of the spread of **vancomycin** resistance will require concerted effort from various departments of the hospital, and can only be achieved if each of the following elements is addressed:

(1) Education of hospital staff regarding the problem of **vancomycin** resistance, (2) early detection and prompt reporting of **vancomycin** resistance in enterococci and other gram-positive microorganisms by the hospital microbiology laboratory, (3) implementation of appropriate infection-control measures to prevent person-to-person transmission of VRE, and (4) prudent **vancomycin** use by clinicians.

Introduction

From 1989 though 1993, the percentage of nosocomial enterococcal infections reported to the CDC National Nosocomial Infections Surveillance (NNIS) System that were resistant to **vancomycin** increased from 0.3% to 7.9%.<SUP>1 The increase was due mainly to the 34-fold rise, from 0.4% to 13.6%, of infections due to VRE in intensive-care unit (ICU) patients, although a trend towards increased **vancomycin** resistance was also noted in non-ICU patients.<SUP>1 The occurrence of VRE in NNIS hospitals was directly associated with larger hospital size (<gr-thn-eq>200 beds) and university affiliation.<SUP>1 Other hospitals also have reported increased endemic rates and clusters of VRE infection and colonization.<SUP>2-6 The actual increase in incidence of VRE in U.S. hospitals may be larger because **vancomycin** resistance, in particular moderate **vancomycin** resistance (as manifested in the VanB phenotype), is not detected consistently with the automated methods used in many clinical laboratories.<SUP>7,8

Vancomycin resistance in enterococci has emerged amidst the increasing incidence of high-level enterococcal resistance to penicillin and aminoglycosides, thus presenting a serious challenge for physicians treating patients with infections due to these microorganisms.<SUP>1,4 Treatment options are often limited to combinations of antimicrobials or experimental compounds with unproven efficacy.<SUP>9

The epidemiology of VRE has not been well elucidated; however, certain patient populations have been found to be at increased risk for VRE infection or colonization; these include critically ill patients or those with severe underlying disease or immunosuppression, such as ICU patients or patients in the oncology or transplant wards; those who have had an intra-abdominal or cardio-thoracic surgical procedure, or indwelling urinary or central venous catheter; and those who have had prolonged hospital stay or received multi-antimicrobial and/or **vancomycin** therapy.<SUP>2-6, CDC unpublished data Because enterococci are part of the normal flora of the gastrointestinal and female genital tracts, most infections with these microorganisms have been attributed to the patient's endogenous flora.<SUP>10 However, recent reports have demonstrated that enterococci, including VRE, can spread by direct patient-to-patient contact or indirectly via transient carriage on hands of personnel<SUP>11 or contaminated environmental surfaces and patient-care equipment.<SUP>12

In addition to the existing problem with VRE, the potential emergence of **vancomycin** resistance in clinical isolates of S. aureus is a serious public health concern. The vanA gene, which is frequently plasmid-borne and confers high-level resistance to **vancomycin**, can be transferred in vitro from enterococci to a variety of gram-positive microorganisms,<SUP>13,14 including Staphylococcus aureus.<SUP>15 Although **vancomycin** resistance in clinical strains of S. epidermidis or S. aureus has not been reported, a **vancomycin**-resistant clinical strain of Staphylococcus haemolyticus has been isolated.<SUP>16

In response to the dramatic increase in **vancomycin** resistance in enterococci, the Subcommittee on the Prevention and Control of Antimicrobial Resistant Microorganisms in Hospitals of the CDC's Hospital Infection Control Practices Advisory Committee (HICPAC) held

meetings on November 14, 1993 and February 18, 1994, with representatives from the American Hospital Association, American Society for Microbiology, Association for Professionals in Infection Control and Epidemiology, Infectious Diseases Society of America, Society for Healthcare Epidemiology of America, and Surgical Infection Society. The Subcommittee members agreed that prompt implementation of control measures is needed and developed recommendations to prevent the spread of VRE. The Subcommittee recognizes that data are limited and considerable research will be required to elucidate fully the epidemiology of VRE and determine cost-effective control strategies, and many U.S. hospitals have concurrent problems with other antimicrobial-resistant organisms, such as methicillin-resistant S. aureus and beta-lactam and aminoglycoside-resistant gram-negative bacilli, that may have different epidemiologic features and require different control methods.

Recommendations

Hospital infection control programs, in collaboration with quality improvement programs, microbiology laboratories, clinical departments, and nursing, administrative, and housekeeping services, should develop a comprehensive, institution-specific, strategic plan to detect, prevent, and control infection and colonization with VRE. It is strongly suggested that the following elements be addressed in the plan.

I. Education Program

Continuing education programs for hospital staff should include information concerning the epidemiology of VRE and the potential impact of this pathogen on the cost and outcome of patient care. Because detection and containment of VRE require a very aggressive approach and high performance standards for hospital personnel, special awareness and educational sessions may be indicated.

II. Role of the Microbiology Laboratory in the Detection, Reporting, and Control of VRE

The microbiology laboratory is the first line of defense against the spread of VRE in the hospital. The laboratory's ability to identify enterococci and detect **vancomycin** resistance promptly and accurately is essential in recognizing VRE colonization and infection and avoiding complex, costly containment efforts that are required when recognition of the problem is delayed. In addition, cooperation and communication between the laboratory and the infection control program will facilitate control efforts substantially.

A. Identification of enterococci: Presumptively identify colonies on primary isolation plates as enterococci by using the colonial morphology, Gram stain, and PYR test. Although identifying enterococci to the species level can help predict certain resistance patterns (e.g., E. faecium is more resistant to penicillin than E. faecalis) and may help determine the epidemiologic relatedness of enterococcal isolates, such identification is not essential if antimicrobial susceptibility testing is performed.

B. Antimicrobial susceptibility testing: Determine **vancomycin** resistance as well as high-level resistance to penicillin and aminoglycosides\17\ for enterococci isolated from blood, sterile body sites (with the possible exception of urine), and other sites as clinically indicated. Evaluate the laboratory's method of susceptibility testing, whether by automated microdilution or disk-

diffusion technique, for its ability to detect **vancomycin** resistance by using E. faecalis ATCC 51299. This strain has a moderate level of **vancomycin** resistance mediated by the vanB gene, which, unlike high-level resistance mediated by vanA, is difficult to detect by most methods used in clinical laboratories. Laboratories using disk diffusion should incubate plates for 24 hours and read zones of inhibition by using transmitted light.\17\,\18\ If testing as above reveals that the method used by the laboratory is inadequate to detect **vancomycin** resistance, the laboratory should perform either of the following:

1. Streak 1 <greek-m>l of standard inoculum (0.5 McFarland) from an isolated colony of enterococci onto BHI agar containing 6 <greek-m>g/ml of **vancomycin**, and incubate the inoculated plate for 24 hours at 35 deg.C. Consider any growth indicative of **vancomycin** resistance.\17\,\18\

2. Determine the minimum inhibitory concentration by agar dilution, broth macrodilution, or manual broth microdilution.\17\,\18\

C. When VRE is isolated from a clinical specimen: 1. Confirm **vancomycin** resistance by repeating antimicrobial susceptibility testing using any of the recommended methods above, particularly if VRE isolates are unusual in the hospital.

2. Immediately, while performing confirmatory susceptibility tests, notify the patient's primary caregiver, patient-care personnel on the ward on which the patient is hospitalized, and infection control personnel regarding the presumptive identification of VRE, so that the patient can be placed on appropriate isolation precautions promptly (See Section III-A-4). Follow this preliminary report with the (final) result of the confirmatory test. Additionally, highlight the report regarding the isolate to alert staff that isolation precautions are indicated.

D. Screening procedures for detecting VRE in hospitals where VRE has not been detected: In many hospital microbiology laboratories, antimicrobial susceptibility testing of enterococcal isolates from urine or nonsterile body sites such as wounds is not performed routinely; thus, recognition of nosocomial VRE colonization and infection in hospitalized patients may be delayed. Therefore, in hospitals where VRE has not yet been detected, special measures can allow earlier detection of VRE.

1. Antimicrobial susceptibility survey. Perform periodic susceptibility testing on enterococcal isolates recovered from all types of clinical specimens, especially from high-risk patients, such as those in an ICU or oncology or transplant ward. The optimal frequency of testing and number of isolates to test are unknown and may vary from hospital to hospital, depending on the hospital's patient population and number of cultures performed. Hospitals processing large numbers of culture specimens will need to test only a small fraction (e.g., 10%) of enterococcal isolates every 1-2 months, whereas hospitals processing fewer specimens may need to test all enterococcal isolates during the survey period. The hospital epidemiologist can be consulted to help design a suitable sampling strategy.

2. Culture survey of stools or rectal swabs. In tertiary medical centers and other hospitals with many critically ill (e.g., ICU, oncology, transplant) patients at high risk for VRE infection or colonization, periodic culture surveys of stools or rectal-swabs of such patients can detect the appearance of VRE. Fecal screening is recommended before VRE infections have been identified clinically because most patients colonized with VRE will have intestinal colonization with this organism.\2\,\4\,\11\ The frequency and intensity of surveillance should be based on the size of the population at risk and the specific hospital unit(s) involved. If VRE have been

detected in other institutions in a hospital's area and/or if a hospital wishes to determine whether VRE is present in the hospital despite the absence of recognized clinical cases, stool or rectal-swab culture surveys are very useful. The cost of screening can be reduced greatly by inoculating specimens onto **vancomycin**-containing selective media\2\,\12\ and restricting screening to those patients who have been in the hospital long enough (e.g., 5-7 days) to have a substantial risk of colonization, or who have been admitted from a facility, such as a tertiary-care hospital or a chronic-care facility, where VRE is known to be present. Once colonization with VRE has been detected, it would be appropriate to begin to screen routinely all of the enterococcal isolates from patients in the hospital (including those from urine and wounds) for **vancomycin** resistance and to intensify efforts to contain VRE spread, i.e., by strict adherence to handwashing and compliance with isolation precautions (See Section III-A-4 below). Intensified fecal screening for VRE may facilitate earlier identification of colonized patients, leading to more efficient containment of the microorganism.

III. Prevention and Control of Nosocomial Transmission of VRE

Eradication of VRE from the hospital is most likely to succeed when VRE infection or colonization is confined to a few patients on a single ward. Once VRE has become endemic on a ward or has spread to multiple wards or to the community, eradication becomes extremely difficult and costly. Aggressive infection control measures and strict compliance by hospital personnel are required to limit nosocomial spread of VRE.

Control of VRE requires a collaborative institution-wide multidisciplinary effort. Therefore, involve the hospital's quality assurance/improvement department at the outset in order to identify specific problems in hospital operations and patient-care systems and to design, implement, and evaluate appropriate changes in these systems.

A. For all hospitals, including those where VRE have been isolated infrequently or not at all:

1. Notify appropriate hospital staff promptly when VRE is detected. (See Section II-C-2 above).

2. Make clinical staff aware of the hospital's policies regarding VRE-infected or colonized patients. Implement the required procedures as soon as VRE is detected because the slightest delay can lead to further spread of VRE and complicate control efforts. Clinical staff play a pivotal role in limiting the spread of VRE in patient-care areas. Accordingly, continuing education is critical regarding the appropriate response to the detection of VRE (See Section I above).

3. Establish system(s) for monitoring appropriate process and outcome measures, such as cumulative incidence or incidence density of VRE colonization, rate of compliance with VRE isolation precautions and handwashing, interval between VRE identification in the laboratory and implementation of isolation precautions on the wards, and the percentage of previously colonized patients admitted to the ward who are promptly recognized and placed on isolation precautions. Relay these data to the clinical, administrative, laboratory, and support staff as reinforcement to ongoing education and control efforts.\19\

4. Isolation precautions to prevent patient-to-patient transmission of VRE:

a. Place VRE-infected or colonized patients in single rooms or in the same room as other patients with VRE.

b. Wear gloves (clean nonsterile gloves are adequate) when entering the room of a VRE-infected or colonized patient; extensive environmental contamination with VRE has been noted in some

studies.<SUP>3,11,20 During the course of caring for a patient, a change of gloves may be necessary after contact with material that may contain high concentrations of VRE (e.g., stool).

c. Wear a gown (a clean nonsterile gown is adequate) when entering the room of a VRE-infected or colonized patient if substantial contact with the patient or environmental surfaces in the patient's room is anticipated, or if the patient is incontinent, or has diarrhea, an ileostomy, a colostomy, or a wound drainage not contained by a dressing.

d. i. Remove gloves and gown before leaving the patient's room, and wash hands immediately with an antiseptic soap.<SUP>4 Hands can be contaminated via glove leaks<SUP>21 or during glove removal and bland soap has been shown to be relatively ineffective in removing VRE from the hands.\22\

ii. Ensure that after glove and gown removal and handwashing, clothing and hands do not contact environmental surfaces potentially contaminated with VRE (e.g., door knob or curtain) in the patient's room.

5. Dedicate the use of noncritical items, such as stethoscope, sphygmomanometer, or electronic rectal thermometer, to a single patient or cohort of patients infected or colonized with VRE.\12\ If such devices are to be used on other patient(s), adequately clean and disinfect them first.\23\

6. Culture stools or rectal swabs of roommates of patients newly found to be infected or colonized with VRE to determine their colonization status, and apply isolation precautions as necessary. Perform additional screening of patients on the ward at the discretion of the infection control staff.

7. Adopt a policy for deciding when patients infected and/or colonized with VRE can be removed from isolation precautions. The optimal requirements remain unknown; however, since VRE colonization may persist indefinitely,\4\ stringent criteria may be appropriate, e.g., VRE-negative results on at least three consecutive occasions, one or more weeks apart, for all cultures from multiple body sites (including stool or rectal swab, perineal area, axilla or umbilicus, and wound, Foley catheter, and/or colostomy sites if present).

8. Establish a system of highlighting the records of infected or colonized patients so that they can be recognized and isolated promptly upon readmission to the hospital because patients with VRE may remain colonized for long periods following discharge from the hospital.

9. Discharging VRE-infected or colonized patients:

Consult local and state health departments in developing a plan regarding the discharge of VRE-infected or colonized patients to nursing homes, other hospitals or home health-care, as part of a larger strategy for handling patients with resolving infections and patients colonized with antimicrobial-resistant microorganisms. This plan should emphasize handwashing and the appropriate use of gloves and gowns when having direct contact with the above-mentioned patients who are transferred from hospitals.

B. In hospitals with endemic VRE or continued VRE transmission despite implementation of measures described in III-A-1 through III-A-9:

1. Focus control efforts initially on ICUs and other areas where VRE transmission rate is highest.\4\ Such units may serve as a reservoir of VRE, from where VRE spreads to other wards when patients are well enough to be transferred.

2. Cohort staff so that nurses and others providing care to patients with VRE do not provide care to noncolonized patients during the same work shift.\4\ Healthcare workers who must provide care to both groups of patients during the same shift should make every effort

to limit their movement between the two patient groups.

3. Carriers of enterococci on the hospital staff have rarely been implicated in the transmission of this organism.\11\ Nonetheless, in conjunction with careful epidemiological studies and upon the direction of the infection control staff, examine personnel for chronic skin and nail problems and perform hand and rectal-swab cultures on them as well as on other personnel providing care to VRE-infected or colonized patients. Remove VRE-positive personnel epidemiologically linked to VRE transmission from the care of VRE-negative patients.

4. The results of several enterococcal outbreak investigations suggest a potential role for the environment in the transmission of enterococci. In one study, nonoutbreak-related strains of **vancomycin**-susceptible enterococci were isolated from cultures of environmental surfaces in patient rooms before and after terminal room cleaning and disinfection.<SUP>CDC unpublished data In institutions experiencing ongoing VRE transmission, verify that the hospital has adequate procedures for the routine care, cleaning, and disinfection of environmental surfaces (e.g., bedrails, charts, carts, doorknobs, faucet handles, bedside commodes) and that these procedures are being followed by housekeeping personnel. Some hospitals may elect to perform focused environmental cultures before and after cleaning of rooms housing patients with VRE to verify the efficacy of hospital policies and procedures. All environmental culturing should be approved and supervised by the infection control program in collaboration with the clinical laboratory.<SUP>11,12,20,24

5. Consider sending representative VRE isolates to reference laboratories for strain typing by pulsed field gel electrophoresis or other suitable techniques to aid in defining reservoirs and patterns of transmission.

IV. Prudent **Vancomycin** Use

Vancomycin use has been reported consistently as a risk factor for colonization and infection with VRE<SUP>2,4,12,25 and may increase the possibility of the emergence of **vancomycin**-resistant S. aureus (VRSA) and/or **vancomycin**-resistant S. epidermidis. Therefore, all hospitals, even those where VRE has never been detected, should develop a comprehensive antimicrobial-utilization plan to provide education for medical staff, oversee surgical prophylaxis, and develop guidelines for the proper use of **vancomycin**. Guideline development should be part of the hospital's quality improvement program and involve participation from the hospital's pharmacy and therapeutics committee, hospital epidemiologist, and infection control, infectious diseases, medical, and surgical staffs. The guidelines should include the following considerations:

A. Situations in which the use of **vancomycin** is appropriate or acceptable:

1. For treatment of serious infections due to beta-lactam resistant gram-positive microorganisms. Clinicians should be aware that **vancomycin** may be less rapidly bactericidal than beta-lactam agents for beta-lactam susceptible staphylococci.<SUP>26,27

2. For treatment of infections due to gram-positive microorganisms in patients with serious allergy to beta-lactam antimicrobials.

3. When antibiotic-associated colitis (AAC) fails to respond to metronidazole therapy or if AAC is severe and potentially life-threatening.

4. Prophylaxis, as recommended by the American Heart Association, for endocarditis following certain procedures in patients at high risk for endocarditis.<SUP>28

5. Prophylaxis for surgical procedures involving implantation of

prosthetic materials or devices at institutions with a high rate of infections due to MRSA or methicillin-resistant S. epidermidis.<SUP>29 A single dose administered immediately before surgery is sufficient unless the procedure lasts more than 6 hours, in which case the dose should be repeated. Prophylaxis should be discontinued after a maximum of 2 doses.<SUP>30-32

B. Situations in which the use of **vancomycin** should be discouraged:

1. Routine surgical prophylaxis.<SUP>30

2. Empiric antimicrobial therapy for a febrile neutropenic patient, unless there is strong evidence at the outset that the patient has an infection due to gram-positive microorganisms (e.g., inflamed exit site of Hickman catheter), and the prevalence of infections due to beta-lactam-resistant gram-positive microorganisms (e.g., MRSA) in the hospital is substantial.<SUP>2,33-39

3. Treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures drawn in the same time frame are negative, i.e., if contamination of the blood culture is likely. Because contamination of blood cultures with skin flora, e.g., S. epidermidis, may cause **vancomycin** to be inappropriately administered to patients, phlebotomists and other personnel who obtain blood cultures should be properly trained to minimize microbial contamination of specimens.

4. Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive microorganisms.<SUP>37,40

5. Systemic or local (e.g., antibiotic lock) prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters or vascular grafts.<SUP>41-46

6. Selective decontamination of the digestive tract.

7. Eradication of MRSA colonization.<SUP>47,48

8. Primary treatment of AAC.<SUP>49

9. Routine prophylaxis for very low-birth-weight infants.<SUP>50

10. Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis.<SUP>51,52

Further study is required to determine the most effective methods for influencing the prescribing practices of physicians, although a variety of techniques may be useful.<SUP>53-56 In addition, key parameters of **vancomycin** use can be tracked through the hospital's quality assurance/improvement process or as part of the drug-utilization review of the pharmacy and therapeutics committee and the medical staff.

V. Detection and Reporting of VRSA

The microbiology laboratory has the primary responsibility for detecting and reporting the occurrence of VRSA in the hospital.

A. Antimicrobial susceptibility testing: Routinely test all clinical isolates of S. aureus for susceptibility to **vancomycin** by using standard methods.<SUP>17

B. When VRSA is identified in a clinical specimen:

1. Confirm **vancomycin** resistance in S. aureus by repeating antimicrobial susceptibility testing using standard methods.<SUP>17 It is advisable to restreak the colony to ensure that the S. aureus culture is pure. The most common causes of false-positive VRSA report are susceptibility testing on mixed cultures and misidentification of VRE, Leukonostoc, S. haemolyticus or Pediococcus as VRSA.<SUP>57,58

2. Immediately, while performing confirmatory testing, notify the hospital's infection control personnel, the patient's primary caregiver, and patient-care personnel on the ward on which the patient is hospitalized so that the patient can be placed promptly on isolation

precautions adapted from, depending on the site(s) of infection or colonization,<SUP>59 those recommended for VRE infection or colonization. (See Section III-A-4 through III-B-5 above.)

3. Immediately notify the state health department and CDC, and send the isolate through the state health department to CDC (telephone number 404-639-1550) for confirmation of **vancomycin** resistance.

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[FR Doc. 94-11913 Filed 5-16-94; 8:45 am]
BILLING CODE 4163-18-P